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LUD 5330.3 DIV (09901357)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	: Rainer Zimmerman et al.
Serial No.	: 09/265,606
Filed	: March 10, 1999
For	: ISOLATED DIMERIC FIBROBLAST ACTIVATION PROTEIN ALPHA, AND USES THEREOF
Group Art Unit	: 1631
Examiner	: N. Ogihara

January 22, 2001

Hon. Commissioner of Patents
and Trademarks
Washington D.C. 20231

RESPONSE
TO OFFICE ACTION
(37 CFR § 1.116)

Sir:

This is submitted in response to the office action of August 25, 2000. A two month extension of time is required, and a request therefor, with fee, accompanies this response.

Claim 5 and 16-19 are pending. No prior art has been cited; however, the examiner has rejected all of these claims under 35 USC § 101 and § 112, first paragraph. Having considered these rejections, applicants traverse.

Claim 5, the only independent claim pending, reads as follows:

> Isolated protein consisting of
> (i) the FAPα catalytic domain, and
> (ii) at least one portion of a non FAPα protein.

The examiner has accepted

> "Applicant's clarification that residues 621-737 constitute the catalytic domain."

Thus, the catalytic domain, i.e., part (i) of claim 5, is 117 amino acids long.

The examiner states that fusion proteins

> "consisting of the FAPα catalytic domain and non-FAPα proteins have not been shown to be functional."

The examiner goes on to state that

> "The use of the claimed FAPα catalytic domain as an immunogen is speculative, as the catalytic domain per se is commonly not available on the surface of a protein, and therefore not likely to be immunogenic."

No support is provided for these assertions. First, the examiner generalizes, apparently that catalytic domains "are not available on protein surfaces," but provides no evidence for this assertion. Further, no evidence is provided with respect to FAPα. Even if the examiner's statements were true, generally, there is no evidence that they could be correlated to the FAPα molecule.

The fact is the claimed molecule is at least 117 amino acid long. Assuming arguendo an average weight per amino acid of 100 daltons, such a molecule is presumably immunogenic. The art is, and has been familiar with, protocols for generating antibodies to molecules much smaller than the molecules in question. See, e.g., Goding Monoclonal Antibodies. Principles and Practices, 2d edition (1986), page 283. This reference represents the state of the art 15 years ago. Immunology has advanced in 15 years.

The examiner argues that

> "The specification has not shown that upon removing the FAPα catalytic domain from the full length FAPα protein, the FAPα catalytic domain is functional or has activity as an independent entity separate from the full length protein."

The proper standard for examination, however, calls upon the PTO to rebut an allegation of utility. Applicants need not, ab initio, provide empirical evidence to support a claim. To the contrary, it is the examiner's burden to show lack of support. The examiner has not done so. Rather, the examiner has proffered unsupported arguments that a fairly large molecule would not be immunogenic, notwithstanding the state of the art, which suggest that it would be.

The examiner has considered applicants arguments based upon Ogata, and dismisses them, arguing that:

> "Ogata et al. have only described the active site residues of DPPIV and Ogata et al. did not show that the DPPIV catalytic domain was active when it stands apart from the entire DPPIV molecule."

With respect to this argument, applicants point out that what Ogata teaches is that GWSYG is the active site for DPPIV. Modification of this sequence abrogates activity.

Applicants require this sequence as part of their molecule. Note Table 2 at page 13 of the specification. Given that Ogata teaches that these residues are key to DPPIV's enzymatic activity, one would assume that their presence in another enzyme suggests that the other enzyme would also work.

To the same end, the fact that Ogata does not each that the catalytic domain is active when removed from DPPIV is irrelevant. Applicants do not have to prove what is asserted. It is the examiner's burden, always, to disprove it.

The examiner points to Geyser as allegedly showing that even conservative substitutions do not correlate with protein activity. This reference is irrelevant to what is being claimed. Applicants have defined a catalytic domain of a full length molecule. The examiner has not challenged the identification of the domain or the fact that the full length molecule is enzymatically active. Presumably, the catalytic domain of a molecule is responsible for that molecule's catalytic activity. Applicants have not claimed substitution or alteration within this domain. Hence, it is the examiner's burden to show, specifically, that the specific material claimed would not function as claimed. No such evidence has been advanced. A prima facie case has not been made out and the rejection cannot be maintained.

Withdrawal of the rejection, and allowance of this application are believed proper and are urged.

Respectfully submitted,

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By _____

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